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12 **EUROPEAN PATENT APPLICATION**

21 Application number: 82305286.5

51 Int. Cl.<sup>3</sup>: C 11 D 1/66

22 Date of filing: 05.10.82

30 Priority: 08.10.81 GB 8130360

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43 Date of publication of application: 20.04.83  
Bulletin 83/16

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54 Designated Contracting States: AT BE CH DE FR GB IT  
LI NL SE

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56 A process for preparing surface-active glycosides and the use of the glycosides in cosmetic, pharmaceutical and household products.

57 Surface active glycosides are made by reaction of mono-  
se or polyose with an alcohol in the presence of an acid cata-  
lyst composition containing acid catalyst and reducing agent;  
the colour properties of the glycosides so made makes them  
attractive for use in cosmetic, pharmaceutical and household  
products. Suitable reducing agents include phosphorous, hy-  
pophosphorous, sulphurous, hyposulphurous, nitrous and hy-  
ponitrous acids. Suitable catalysts include the known etherifi-  
cation catalysts.

**EP 0 077 167 A1**

A PROCESS FOR PREPARING SURFACE-ACTIVE  
GLYCOSIDES AND THE USE OF THE GLYCOSIDES  
IN COSMETIC, PHARMACEUTICAL AND HOUSEHOLD  
PRODUCTS

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This invention is concerned with the process of manufacture of glycosides from alcohols and poly and/or mono saccharides and the use of said glycosides in cosmetic, pharmaceutical and household products. Typical products of the reaction are mixtures of substituted monosaccharides and substituted poly-, mostly oligosaccharides, with surface-active and such colour properties as to enable them to be used in cosmetic, pharmaceutical and household products.

The glycosides to which the invention relates are generally a mixture of various monomeric and oligomeric materials and are non-ionic surface agents which possess:

- high foaming power
- emulsifying properties
- softening and detergent properties.

These products are readily biodegraded.

In this specification we intend the prefix "oligo" to include as many as eleven repeating units. Alkylsaccharides are molecules which have been known for many years, since Fischer described them in 1909, but their method of manufacture, resulting in specific products, was too difficult or too costly for them to be developed industrially.

The methods used consisted of:

- reacting acetic anhydride with glucose to form glucose pentacetate, then transforming this product to bromo-tetracetate by the action of hydrobromic acid. The reaction of this glucose bromotetracetate with a fatty alcohol in the presence of silver

oxide results in glucoside tetracetate which only requires hydrolysis for glucoside to be obtained.

- 5 - reacting glucose pentacetate, prepared as above, with a fatty alcohol in the presence of zinc chloride, which again results in glucoside tetracetate, again requiring hydrolysis.

- 10 In 1965 a process for preparing ethers from glucose fatty alcohols was described in USP 3,170,915 (Monsanto). This method consists of reacting a sugar with sodium methylate in dimethyl sulphoxide and making a halogenised paraffin react on the soda derivate obtained.

- 15 These processes are too expensive and yield will defined products.

- 20 In 1965 Rohm and Haas, described in USP 3,219,656 a process for manufacturing glucosides by transesterification between a methylglucose and heavier alcohols. In fact, the etherification of sugars by methyl alcohol is readily achieved by the conventional etherification processes and results in a methylglucose which is considerably more stable with regard to heat and oligomerisation than glucose.

- 25 The Rohm and Haas process consists of transesterifying this methylglucose using butyl alcohol in order to obtain butyl ether from the glucose which is itself transesterified with the aid of a fatty alcohol, these two reactions being carried out in the  
30 presence, as a catalyst, of a cation-exchanging resin of a type such as those described in USP 3,037,052 in the name of the same firm. This process, although

less expensive, still requires the consecutive elimination of two light alcohols with the cost these two operations entail, and the unavoidable loss of solvent.

5 In 1974, in USP 3,839,318, Rohm and Haas described the preparation of a mixture of mono-substituted mono-saccharide and mono-substituted oligosaccharide obtained by a direct reaction of a fatty alcohol and a monosaccharide in the presence of an excess  
10 of alcohol and an acidic catalyst such as sulphuric acid, nitric acid, hydrochloric acid, sulphonic acid, at a temperature of 80 to 130°C.

The reaction conditions are defined very precisely so that the basic monosaccharide is not subjected  
15 to too high a level of degradation during the course of condensation.

The excess of fatty alcohol relative to the mono-saccharide must be sufficient; the level of excess required becomes greater as the molecular weight  
20 of the alcohol increases. A curve is attached to this prior specification showing the minimum excess of fatty alcohol to be used, as a function of the number of carbon atoms contained in the molecule.

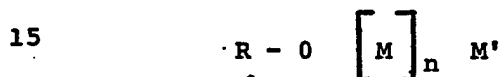
This process yields a mixture of glycosides possessing  
25 very useful surface-active properties, a high level of stability to salts and alkaline agents, but the colour of the mixture is too deep for it to be used in the cosmetic or pharmaceutical industries, or for formulating products for domestic use, without  
30 purification or extensive decoloration with the aid of powerful oxidants.

We have now found a process which is capable of preparing such a mixture of fatty alcohol ethers and

mono- and oligo-saccharides which yields a useful surface-active product, and the purity and coloration of which allow it to be used in cosmetic and pharmaceutical products and for the formulation of products for household use without a subsequent decolorisation step.

The advantages of eliminating the decoloration step are not only economic but also from the aspect of the quality of the product, as this decoloration process entails the formation of unstable oxidised products which may later result in modification of the colour or the pH.

This invention relates in particular to glycosides of the structure:



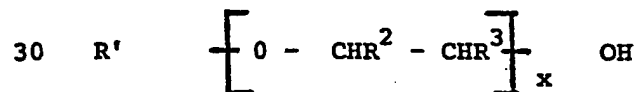
wherein:

n is preferably 0 to 10 but may be much higher, for example such as would result from the reaction of hydrolysed starch or cellulose,

M and M' represent the same or different monose or polyose residues which in the case of M may be a mixture,

R is

- a) a linear paraffinic chain containing 8 to 18 carbon atoms;
- b) a branched primary or secondary hydrocarbon chain containing 8 to 18 carbon atoms; or
- c) a radical of the formula:



wherein:

x is 1 to 8, and R' is

- a linear paraffinic chain;
- a branched hydrocarbon chain; or
- a monoalkyl or dialkylphenol,

and  $R^2$  and  $R^3$  are either both hydrogen or one is  
5 hydrogen and the other is methyl.

In the above "monose" means mono-aldose or mono-ketose

According to our invention surface active glycosides  
are prepared by reacting an alcohol with an aldose or  
ketose in the presence of an acid catalyst composition  
10 comprising an acid catalyst and a reducing agent.

Suitable catalysts are any acid catalysts known to  
be useful in etherification reactions such as  
sulphuric acid, hydrochloric acid, nitric acid,  
sulphonic acid and strong acid cation exchange resins.

15 Suitable reducing agents include acid reducing  
agents such as phosphorous hypophosphorous,  
sulphurous, hyposulphurous, nitrous and hyponitrous  
acid, which are preferred. These may be used in the  
form of their salts as long as the overall catalyst  
20 plus reducing agent composition remains acid.

The reaction time necessary for etherification depends  
on such normal factors as the catalyst used, its  
quantity and the temperature.

25 The conditions described in U.S. Patent 3,839,318 may  
appropriately be used in this invention. They  
generally indicate the optimum and an acceptable  
balance between quality and the price of the product  
obtained.

30 The ratio of fatty alcohol to aldose or ketose lies  
between 4 to 1 and 1.25 to 1 by mole.

The reaction temperature is preferably 80 to 130°C.

The quantity of catalyst plus reducing agent is  
preferably 0.03 to 10% of the weight of the charged

aldose and/or ketose.

Under these conditions and without/modify<sup>significantly</sup>ing the reaction speed it is possible to obtain a less coloured condensation product using the invention than when the reducing agent is absent as in the prior art.

It has been further shown that the addition of a reducing acid to the usual etherification catalyst allows, without modifying the speed of reaction, the quantity of catalyst to be reduced. The speed of reaction obtained by using 0.014 moles of sulfuric acid per mole of glucose can for example be maintained by replacing half of this acid by hypophosphorous acid (0.007 moles).

Furthermore, while it is clearly desirable, whatever the catalyst, to remove the excess alcohol as quickly as possible, so as to minimise the time for which the reaction product is subjected to elevated temperature, it is preferable to effect this removal in the presence of the reducing agent so as to minimise colour deterioration still further.

This elimination of excess alcohol can be accomplished, by one of the known methods such as vacuum distillation, molecular distillation and thin film evaporation.

Suitable alcohols include fatty alcohols ( $C_{10}$  and above) and they may be linear or branched, primary or secondary. The alcohols may contain in their molecules phenyl, alkylphenyl or alkoxy radicals.

The ketoses and aldoses which may be used in this process may be monoses or polyoses for example suitable monoses include arabinose, galactose, glucose,



mannose, ribose and xylose and suitable polyoses include saccharose, maltose, lactose and raffinose, as well as saccharides obtained by hydrolysis of higher polysaccharides such as starch and cellulose.

- 5 The glycosides obtained by this process are generally transparent, vitreous solids with a sticky surface. They may be diluted with water so that they can be presented commercially in the form of an aqueous solution.
- 10 The following Examples of some embodiments of the invention are given for the purpose of illustration only.

EXAMPLE 1

A mixture containing:

- 15 732.5 g of an n-octanol and n-decanol 45/55 mixture (5 moles)  
360 g of glucose (2 moles)  
1.4 g of 98% sulphuric acid (0.014 moles)  
1.85 g of 50% hypophosphorous acid (0.014 moles)
- 20 is processed for 6 hours at 95°C in a vacuum at 40 mm of mercury. The solution obtained (in the excess of alcohol) after centrifuging to eliminate approximately 0.5% of non-reacted glucose has a monoalkylglucoside content of 19% and a VCS of 3.
- 25 This mixture is neutralised to a pH of 4 - 6 using caustic soda, and the excess of fatty alcohol is eliminated by vacuum stripping.
- The product obtained in a 70% solution in water has a colour of VCS 6, and its aqueous solution at 5%
- 30 has a pH of 5.

COMPARATIVE TEST A

A product with a composition similar to that of Example 1, prepared according to the process described

in USP 3,839,318, using the same amounts  
n-octanol, n-decanol and glucose as in Example 1  
with 0.02 moles of sulphuric acid and no hypo-  
phosphorous acid yielded a glucoside with a colour  
5 of VCS 17 to 18 having been stripped by the same  
process as in Example 1. The monoglucoside content  
and the reaction speed are the same in the two cases,  
although the quantity of sulphuric acid used is  
two times less in the present example.

10 EXAMPLE II

A mixture containing:

732.5 g of a 45/55 mixture of n-octanol and n-  
decanol (5 moles)

360 g of glucose (2 moles)

15 1.4 g of 98% sulphuric acid (0.014 moles)

3.44 g of 50% hypophosphorous acid (0.026 moles)

is processed under the same operating conditions.

The product obtained has a colour of VCS 6 in a  
70% solution in water, and its 5% solution in

20 water has a pH of 3.3.

EXAMPLE III

A mixture containing:

732.5 g of a 45/55 mixture of n-octanol and n-decanol  
(5 moles)

25 360 g of glucose (2 moles)

1.4 g of 98% sulphuric acid (0.014 moles)

6.88 g of 50% hypophosphorous acid (0.052 moles)

is processed under the same conditions as in Example I.

The 70% solution in water obtained has a colour of

30 VCS 5 and its 5% aqueous solution has a pH of 2.9.

EXAMPLE IV

A mixture containing:

510 g of n-hexanol (5 moles)

360 g of glucose (2 moles)  
1.4 g of 98% sulphuric acid (0.014 moles)  
1.85 g of 50% hypophosphorous acid (0.014 moles)

is processed according to the process described in

5 Example I.

The product obtained is a mixture of hexylglucose and hexylolisoglucoside with a colour of VCS 5 to 6.

EXAMPLE V

A mixture containing:

- 10 732.5 g of a 45/55 mixture of n-octanol and n-decanol  
(5 moles)

360 g of fructose (2 moles)  
1.4 g of 98% sulphuric acid (0.014 moles)  
1.85 g of 50% hypophosphorous acid (0.014 moles),

- 15 processed according to the process described in  
Example I, yields a fructoside with a colour of  
VCS 6 in a 70% aqueous solution.

This product is endowed with the same surface-active  
properties as the glucose derivative.

20 EXAMPLE VI

A mixture containing:

790 g of n-decanol (5 moles)  
360 g of glucose (2 moles)  
4 g of 98% sulphuric acid (0.04 moles)

- 25 1.3 g of sodium hypophosphite (0.014 moles),

processed according to the process described in  
Example I, yields a glucoside with a colour of VCS 6  
in a 70% aqueous solution.

EXAMPLE VII

- 30 A mixture containing:

732.5 g of a 45/55 mixture of n-octanol and n-decanol  
(5 moles)

360 g of glucose (2 moles)

1.4 g of sulphuric acid (98%) (0.014 moles)

and

1.328 g sodium metabisulphite (0.007 moles)

5 is processed for 6 hours at 95°C in a vacuum of 40 mm of mercury.

The reaction product, after neutralisation to a pH of 4 to 6, was treated under vacuum until elimination of excess alcohol.

10 The glucoside obtained had, in 70% aqueous solution, a VCS colour of 6.

#### EXAMPLE VIII

A mixture containing:

732.5 g of a 45/55 mixture of n-octanol and

15 n-decanol (5 moles)

360 g of glucose (2 moles)

0.7 g of 98% sulphuric acid (0.007 m) and

0.925 g of 50% hypophosphorous acid (0.007 m)

is processed according to the process described in Example 1. The percent solids (vol/vol) in the reacting mixture is measured every hour, the falling value of this percentage indicating progress of the reaction towards completion. The results of these measurements, together with the VCS colour in 70% solution of the product, are given in Table I.

25 Comparative Examples B and C

Example VIII is repeated except that the sulphuric acid and hypophosphorous acid in the Example are replaced by the indicated amounts of sulphuric acid alone, as given in Table 1.

30 From the Table it can be seen that the rate of reaction according to the invention was not significantly below the best of the Comparative Examples but the colour was significantly improved.

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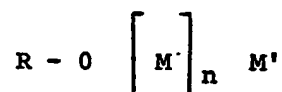
- 11 -

TABLE 1

Experiment:	Comparative Example B	Comparative Example C	Example VIII
mole ratio acid/ glucose	0.014 H <sub>2</sub> SO <sub>4</sub>	0.007 H <sub>2</sub> SO <sub>4</sub>	0.007 H <sub>2</sub> SO <sub>4</sub> 0.007 H <sub>3</sub> PO <sub>2</sub>
time (hours)	Percent solids in the mixture (vol./vol.)		
1	40	56	44
2	10	40	34
3	0.5	12	5
4	0.3	6	1.5
5	0.2	1.2	0.7
6	0.1	0.5	0.3
VCS of product concentrated to 70% aqueous solution	> 18	14	11

CLAIMS:

1. A process for the preparation of surface active glycosides which comprises reacting an alcohol with an aldose or ketose in the presence of an acid catalyst composition comprising an acid catalyst and a reducing agent.
2. A process as claimed in claim 1 in which the glycoside has the structure:



wherein:

n is 0 or an integer,

M and M' represent the same or different monose or polyose residues which in the case of M may be a mixture,

R is

- a) a linear paraffinic chain containing 8 to 18 carbon atoms;
- b) a branched primary or secondary hydrocarbon chain containing 8 to 18 carbon atoms; or
- c) a radical of the formula:



wherein:

x is 1 to 8, and R' is

- a linear paraffinic chain;
- a branched hydrocarbon chain; or
- a monoalkyl or dialkylphenol,

and R<sup>2</sup> and R<sup>3</sup> are either both hydrogen or one is hydrogen and the other is methyl.

3. A process as claimed in Claim 2 wherein n is 0 to 10 or a number such as would result from the reaction of hydrolysed starch or cellulose.

4. A process as claimed in any preceding claim  
5 wherein the ratio of alcohol to aldose and/or ketose is from 4 to 1 to 1.25 to 1 by mole.

5. A process as claimed in any preceding claim which is carried out at a temperature of 80 to 130°C.

6. A process as claimed in any preceding claim  
10 wherein the quantity of catalyst plus reducing agent is 0.03 to 10% by weight of the weight of aldose and/or ketose.

7. A process as claimed in any preceding claim wherein the reducing agent comprises phosphorous,  
15 hypophosphorous, sulphurous, hyposulphurous, nitrous and/or hyponitrous acid and/or salt(s) thereof.

8. A process as claimed in any preceding claim wherein excess alcohol is removed from the reaction  
20 products in the presence of the reducing agent.

9. The use of a glycoside made by a process as claimed in any preceding claim in cosmetic, pharmaceutical or household products.



European Patent  
Office

# EUROPEAN SEARCH REPORT

0077167

Application number

EP 82 30 5286.5

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int. Cl. 3)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
Y	<u>DE - A - 2 036 472</u> (ATLAS CHEMICAL INDUSTRIES INC.) * claims 1, 8, 9 *	1,7	C 11-D 1/66
Y	<u>DE - A - 1 905 523</u> (ATLAS CHEMICAL INDUSTRIES INC.) * claims 1, 5 *	1,7	
D,Y	<u>US - A - 3 839 318</u> (R.C. MANSFIELD) * claim 1 *	1,7	TECHNICAL FIELDS SEARCHED (Int.Cl. 3)
D,A	<u>US - A - 3 219 656</u> (F.E. BOETTNER) * claims 1, 5 *		C 11 D 1/00
			CATEGORY OF CITED DOCUMENTS
			X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background O: non-written disclosure P: intermediate document T: theory or principle underlying the invention E: earlier patent document, but published on, or after the filing date D: document cited in the application L: document cited for other reasons
Y	The present search report has been drawn up for all claims		&: member of the same patent family, corresponding document
Place of search Berlin		Date of completion of the search 27-12-1982	Examiner SCHULTZE